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10/59  
Prof. J. Lederberg  
Dept. of Genetics  
Stanford University  
Stanford California

Dear Professor Lederberg,

I received your letter and have sent you (printed matter) the papers: Schäfler a. Beneș - Ann.Inst. Pasteur, 1959, 96, 231, and Schäfler a. Schäfler, idem 790. The article of J. Bacteriol., will be sent immediately after receive of reprints. The reprints I have sent you represent a rezumative form of some more ample papers and the mutative fermentations is described in them only in standpoint of taxonomic interrelations. I am always at your disposal for supplementary data.

My impression is that from the mutative fermentations studied by us,  $\beta$ -glucosidase in E.freundii and Salmonella described in the papers I have sent you, and the  $\beta$ -glucosidase in E.coli could present some interest from the genetical standpoint. In E.coli, the exclusive mutative fermentation of salicine takes place with a greater frequency than that of arbutine and specially of cellobiose. The arbutine<sup>+</sup> forms are also salicine<sup>+</sup>, the reverse is only partially valid. In the studied Enterobacteriaceae the fermentative complex of  $\beta$ -glucosidases seems to be formed of several related genetic steps which could be relatively easily differentiated by the hydrolysed substrate?

In continuation of the study of lactose fermentation by Salmonella, 2 papers are in press, in the "Reports of Akad.Sci.USSR" (in Russian) and "J.Bacteriol." In these papers is described the influence of the substratum concentration on the frequency of the appearance of lactose<sup>+</sup> mutants and an unspecific inhibition by glutamic acid, serine, succinate and other nutritive substances easily utilisable as carbon source of the adaptive fermentation of lactose by L<sup>+</sup> variants, probably by concurrence for metabolites from metabolic pool. This as well as the smaller growth rate of the L<sup>+</sup> variants in conditions in which they are unable to utilize lactose determines the impossibility to obtain these variants in some richer culture media. Analogous phenomena seem

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to exist also in case of some weak fermentations (salicine by Salmonella and some E. freundii strains par ex.). For evidencing the real fermentative capacity of a strain it is sometimes necessary that it should be simultaneously incubated as well on poor media (liquid and solid with ammonium salts) as on rich media. I will send you reprints after the issue of the papers.

Now I would ask your opinion in relation of some of your works. I read with very great interest your papers on "Replica plating". In case of antibiotic and bacteriophage resistance could be indirectly selected metabolic modified mutants (which theoretically can appear also under the influence of culture medium) in which the resistance is an epiphenomenon. The papers of Fusillo seem to suggest in some cases this hypothesis. For these reasons it seems that the experiments described in literature on the indirect selection of fermentative mutants could present more sureness from the standpoint of interpretation of results. Surer results could be perhaps reached if by replica plating would be selected the capacity to form inducible enzymes (par ex.  $\beta$ -galactosidase in E. coli mutabile). Induction of enzyme in the population which has not been in contact with lactose, could be realised in this case with another inductor, melibiose par ex., which is not a substratum for this enzyme. Your opinion on this type of experiences would highly interest me.

With kindest regards,

yours sincerely

*S. Schäfler*

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